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Date: August 16, 2004

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Our Docket No. CMCC 779

Client/Matter No. 078856/47

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## MESSAGE:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Samy Ashkar

Serial No.: 09/981,845

Art Unit: 1647

Filed: October 18, 2001

Examiner: Regina M. Deberry

For: OSTEOPONTIN-COATED SURFACES AND METHODS OF USE

(45048308.1)

Incomplete  
missing p. 10-34

PTO/SB/21 (08-03)

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<b>TRANSMITTAL FORM</b> (to be used for all correspondence after initial filing)	Application Number	09/ 981,845
	Filing Date	October 18, 2001
	First Named Inventor	Samy Ashkaar
	Art Unit	1647
	Examiner Name	Regina M. Deberry
Total Number of Pages in This Submission	Attorney Docket Number	CMCC 779

ENCLOSURES (Check all that apply)		
<input checked="" type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____	<input type="checkbox"/> After Allowance communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input checked="" type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): 3 references-2 papers and 1 abstract
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Firm or Individual name	Patrea L. Pabst Esq., Reg. No. 31,284 Pabst Patent Group LLP 400 Colony Square, Suite 1200, Atlanta, GA 30361	
Signature	_____	
Date	August 16, 2004	

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Effective 10/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27**TOTAL AMOUNT OF PAYMENT** (\$165.00)**Complete if Known**

Application Number	09/981,845
Filing Date	October 18, 2001
First Named Inventor	Samy Ashkar
Examiner Name	Regina M. Deberry
Art Unit	1647
Attorney Docket No.	CMCC 779

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Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1001 7/0	2001 3/5	Utility filing fee	
1002 3/0	2002 1/0	Design filing fee	
1003 5/0	2003 2/5	Plant filing fee	
1004 7/0	2004 3/5	Reissue filing fee	
1005 1/0	2005 80	Provisional filing fee	
<b>SUBTOTAL (1)</b>			<b>(\$)</b>

**2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE**

Total Claims: 6 -20\* =    X    =   

Independent Claims: 1 -3\*\* =    X    =   

Multiple Dependent:    X    =   

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1202 18	2202 9	Claims in excess of 20	
1201 8/5	2201 4/3	Independent claims in excess of 3	
1203 2/0	2203 1/5	Multiple dependent claim, if not paid	
1204 8/5	2204 4/3	** Reissue independent claims over original patent	
1205 1/5	2205 9	** Reissue claims in excess of 20 and over original patent	
<b>SUBTOTAL (2)</b>			<b>(\$)</b>

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**FEE CALCULATION (continued)****3. ADDITIONAL FEES**

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1051 130	2051 85	Surcharge - late filing fee or oath	
1052 50	2052 25	Surcharge - late provisional filing fee or cover sheet	
1053 130	2053 130	Non-English specification	
1812 2,520	1812 2,520	For filing a request for ex parte reexamination	
1804 920*	1804 920*	Requesting publication of SIR prior to Examiner action	
1805 1,840*	1805 1,840*	Requesting publication of SIR after Examiner action	
1251 110	2251 55	Extension for reply within first month	
1252 420	2252 210	Extension for reply within second month	
1253 950	2253 475	Extension for reply within third month	
1254 1,480	2254 740	Extension for reply within fourth month	
1255 2,010	2255 1,005	Extension for reply within fifth month	
1401 330	2401 165	Notice of Appeal	
1402 330	2402 165	Filing a brief in support of an appeal	165.00
1403 290	2403 145	Request for oral hearing	
1451 1,510	1451 1,510	Petition to institute a public use proceeding	
1452 110	2452 55	Petition to revive - unavoidable	
1453 1,300	2453 665	Petition to revive - unintentional	
1501 1,310	2501 665	Utility issue fee (or reissue)	
1502 480	2502 240	Design issue fee	
1503 640	2503 320	Plant issue fee	
1460 130	1460 130	Petitions to the Commissioner	
1807 50	1807 50	Processing fee under 37 CFR 1.17(i)	
1806 180	1806 180	Submission of Information Disclosure Stmt	
8021 40	8021 40	Recording each patent assignment per property (times number of properties)	
1809 770	2809 385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810 770	2810 385	For each additional invention to be examined (37 CFR 1.129(b))	
1801 770	2801 385	Request for Continued Examination (RCE)	
1802 900	1802 900	Request for expedited examination of a design application	

Other fee (specify) \_\_\_\_\_

\*Reduced by Basic Filing Fee Paid

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(Attorney/Agent)

31.284

(Complete if applicable)

Telephone (404) 879-2151

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Date August 16, 2004

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Appellants: Samy Ashkar and Jairo Salcedo

Serial No.: 09/981,845

Art Unit: 1647

Filed: October 18, 2001

Examiner: Regina M. Deberry

For: *OSTEOPONTIN-COATED SURFACES AND METHODS OF USE*

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P.O. Box 1450  
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**APPEAL BRIEF**

Sir:

This is an appeal from the final rejection of claims 1-6 in the Office Action mailed February 13, 2004, in the above-identified patent application. A Notice of Appeal was mailed on June 14, 2004 (there is an error in the Advisory Action mailed June 28, 2004). The Commissioner is hereby authorized to charge \$165.00, the fee for the filing of this Appeal Brief for a small entity, to Deposit Account No. 50-3129. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

**(1) REAL PARTY IN INTEREST**

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The real party in interest of this application is Children's Medical Center Corporation in Boston, MA, the assignee of record; and the licensee of record OraPharma, Inc. in Warminster, PA.

**(2) RELATED APPEALS AND INTERFERENCES**

There are no related appeals or interferences known to appellant, the undersigned, or appellant's assignee which directly affects, which would be directly affected by, or which would have a bearing on the Board's decision in this appeal.

**(3) STATUS OF CLAIMS ON APPEAL**

Claims 1-6 are pending. Claims 1-6 are on appeal. Claims 7-18 were cancelled in an Amendment filed on November 21, 2003. The text of each claim on appeal, as pending, is set forth in an Appendix to this Appeal Brief.

**(4) STATUS OF AMENDMENTS**

An amendment after final rejection was mailed on May 11, 2004. In the Advisory Action mailed June 28, 2004, the Examiner indicated that this amendment would be entered. An appendix sets forth the claims on appeal.

**(5) SUMMARY OF THE INVENTION**

The claims are drawn to isolated active osteopontin fragments and osteopontin-derived peptide fragments that have cell-attachment and cell-spread activity (page 7, line 23 to page 8, line 12). The peptide fragments may be used to increase cell attachment to a material, as well as enhance cell spread on the material (page 11, lines 9-18). The material is suitable for use on a material which is implanted into a patient to enhance cell-attachment and cell-spread activity and

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thereby integration of the implant, for example, for use in treatment of periodontal disease (page 10, lines 16-23). Claim 1 is directed to an osteopontin-derived peptide fragment comprising an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, and SEQ ID NO:15 (page 8, lines 7-26 and page 12, lines 4-13). Claim 2 is directed to the peptide fragment of claim 1, wherein the peptide increases cell attachment to a material and increases cell spread (page 8, lines 11-12 and page 53, lines 12-17). Claim 3 is directed to the peptide fragment of claim 2, wherein the peptide binds to at least one receptor on a cell surface. Claim 4 is directed to the peptide fragment of claim 3, wherein the receptor(s) is an integrin. Claim 5 is directed to the peptide fragment of claim 4, wherein the integrin(s) is  $\alpha_v\beta_3$ ,  $\alpha_v\beta_5$ ,  $4\beta_1$ ,  $2\beta_1$ , VCAM, ICAM CD44, or  $V_3V_x$ . Support for claims 3, 4, and 5 can be found on page 3, line 27 to page 4, line 14 and page 53, lines 17-21. Claim 6 is directed to the peptide fragment of claim 3 wherein the cell is an osteoprogenitor cell, tumor cell, macrophage, periosteal cell, endothelial cell, epithelial cell, eosinophil, stem cell, limited potential precursor cell, precursor cells committed precursor cell, or differentiated cell (page 8, line 29 to page 9, line 2).

**(6) ISSUES ON APPEAL**

The issues presented on appeal are:

- (1) whether claims 1-6 are enabled under 35 U.S.C. § 112, first paragraph.

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(7) ARGUMENTS

(a) The Claimed Invention

The claims are directed to active osteopontin-derived peptide fragments and their use in and/or on materials to increase cell attachment and cell spread activity. The peptides may be used to coat, for example, a surgical implant where cell attachment and growth on the implant are desirable. The peptide fragments comprise the sequences

VFTPVVPTVDTYDGRGDSVVYGLRSKSKKFRRP (SEQ ID NO. 7),  
RSRRATEVFTPVVPTVDTYDGRGDSVVYGLRSKSKKFRRP (SEQ ID NO:8),  
SDELVTDFPTDLPATEVFTPVVPTVDTYDGRGDSVVYGLRSKSKKFRRP (SEQ ID NO:9),  
RSRRATEVFTPVVPTVDTYDGRGDSVVYGRRSKSKKFRRP (SEQ ID NO:10),  
RSRRATEVFTPVVPTVDTYDGRGDSVVYGRRSKSKKFRRPAGAAGGPAGPAG  
PAGPAGPAGPA (SEQ ID NO:11), RSRRVFTPFIPITESANDGRGDSVAYGLKSKSKKFRR  
(SEQ ID NO:12), DTFTPIVPTVDVPNGRFDLAYGLKSKSKKFQ (SEQ ID NO:13),  
RSRRATEVFTPVVPTVDTYDGRADSVVYGRRSKSKKFRRP (SEQ ID NO:14), and acetyl-  
RSRRATEVFTPVVPTVDTYDGRGDSVVYGLRSKSKKFRRP (SEQ ID NO:15).

The osteopontin-derived peptide fragments increase cell binding and spread by binding to integrins, such as  $\alpha_v\beta_3$ ,  $\alpha_v\beta_5$ ,  $4\beta_1$ ,  $2\beta_1$ , VCAM, ICAM CD44,  $V_3V_5$ , on the surface of cells. The peptide fragments may be used to modulate a number of different cell types, including osteoprogenitor cells, tumor cells, macrophages, periosteal cells, endothelial cells, epithelial cells, eosinophils, stem cells, limited potential precursor cells, precursor cells, committed precursor cells, and differentiated cells.

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The peptides have numerous applications, but principally in tissue repair or regeneration, for example, when coated onto a titanium material and used in the treatment of periodontal disease to enhance bone regrowth.

**(b) Rejection of claims 1-6 Under 35 U.S.C. § 112, first paragraph**

***The Legal Standard***

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art as of the date of filing, without undue experimentation (*See, e.g., Amgen v. Hoechst Marion Roussell* 314 F.3d 1313 (Fed. Cir. 2003); *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d at 165, 42 USPQ2d at 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *See also In re Fisher*, 427 F.2d at 839, 166 USPQ at 24; *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343 (CCPA 1976)). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (*M.I.T. v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985)). As affirmed by the Court in *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524 (Fed. Cir. 1987), a patent need not teach, and preferably omits, what is well known in the art.

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. *See In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in *Wands*, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the



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quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. In cases that involve unpredictable factors, "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' *Atlas Powder Co., v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir.1984). There is no requirement for examples.

#### *Analysis*

A proper analysis of the *Wands* factors shows that claims 1-6 satisfy the enablement requirement. The quantity of experimentation necessary to make and use the claimed peptides is **not undue**. The claims are directed to osteopontin-derived peptide fragments comprising SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, or SEQ ID NO:15. These sequences are well known. The amino acid sequence and structure of osteopontin, from which the peptide fragments are derived, are well known. One skilled in the art would have no difficulty making short peptides synthetically, or longer peptides using a portion of the nucleotide sequence encoding osteopontin. The point of novelty is the identification of the amino acid sequence in a very large protein which has the desired activity, and that this activity is retained even in a very small peptide relative to the huge

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protein from which it is derived. The specification describes how to coat the peptides to a material (page 13, line 14 to page 14, line 21) and describes the types of materials that may be coated (page 10, lines 16-23 and page 14, lines 22-28). The specification describes the cell types that may be regulated using the osteopontin-derived peptides fragments (page 8, line 29 to page 9, line 2) and that the peptides bind integrin receptors on the surface of these cells (page 3, line 27 to page 4, line 14).

Although there is no requirement for examples, Example 12 and Table 8 on pages 53-55 of the originally filed application, demonstrate that each of SEQ ID NO:15, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or SEQ ID NO:14 binds to osteoprogenitor cells and significantly increases cellular attachment and spread over the control. In addition, Example 12 and Table 8 illustrate that antibodies to integrins (i.e.,  $\alpha_v\beta_3$ ) inhibit the percentage of attached cells and cell spread induced by the peptides (i.e., SEQ ID NO: 15), indicating that the peptides interact with integrins.

The guidance in the specification and ease in carrying out the assays, as shown in the  
PAGE 10/10 \* RCVD AT 8/16/2004 10:25:09 PM [Eastern Daylight Time] \* SVR:USPTO-EFXXRF-1/0 \* DNIS:8729306 \* CSID:706 283 7737 \* DURATION (mm-ss):03-42